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Regular paper

Acupuncture attenuates cognitive impairments in vascular dementia through inhibiting miR-143-3p

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Background: **Acupuncture can be used to treat vascular dementia (VD), but the underlying mechanism remains unclear. This study aimed to investigate the expression and clinical significance of microRNA-143-3p (miR-143-3p) in VD patients and explore whether acupuncture ameliorates VD by regulating miR-143-3p. Methods**: **Cognitive function and daily living ability in VD patients were assessed by mini-mental state examination, Hasegawa's dementia scale and activities of daily living scale, respectively. VD model of male Wistar rats was established using permanent bilateral common carotid artery occlusion. The expression level of miR-143-3p was measured by quantitative real-time PCR. Morris water maze test was used to assess the cognitive function of VD rat model. Receiver operating characteristic analysis was used to assess the diagnostic value of miR-143-3p in VD patients. Correlations between variables were analyzed by Pearson's correlation analysis. Results**: **Increased serum miR-143-3p expression in VD patients had a high diagnostic value to screen VD patients. Serum miR-143-3p level in VD patients after acupuncture treatment was decreased. After acupuncture treatment, serum miR-143-3p was negatively correlated with cognitive function and daily living ability in VD patients. miR-143-3p level was increased in VD rats, and the suppressive effects of acupuncture on miR-143-3p levels were relieved by miR-143-3p mimic. Overexpression of miR-143-3p reversed the ameliorative effect of acupuncture on cognitive functions of VD rats. Conclusion**: **Serum miR-143-3p expression is upregulated in VD patients and downregulated in VD patients after acupuncture treatment. Additionally, acupuncture treatment may attenuate cognitive impairments in VD by suppressing miR-143-3p.**

Keywords: acupuncture; miR-143-3p; vascular dementia; cognitive function

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Abbreviations: ADL, activities of daily living; HDS-R, Hasegawa's dementia scale; HOXA1, homeobox A1; miR-143-3p, microRNA-143-3p; miRNAs, microRNAs; MMSE, mini-mental state examination; MWM, Morris water maze; NRG1, neuregulin-1; PTPN1, tyrosine-protein phosphatase non-receptor type 1; PUMA, P53-up-regulated modulator of apoptosis; qRT-PCR, quantitative real-time PCR; ROC, receiver operating characteristic; TCM, traditional Chinese medicine; VD, vascular dementia; 2VO, permanent bilateral common carotid artery occlusion

INTRODUCTION

Vascular dementia (VD) refers to a severe cognitive dysfunction syndrome resulting from ischemic stroke, hemorrhagic stroke, and cerebrovascular disease causing hypoperfusion in brain regions such as memory, cognition, and behavior. As a multiple disease of the elderly, VD is the second most common type of dementia. It damages people's learning, memory, language, reasoning, and executive functions and may also impair motor and autonomic functions. Although there are many treatments, the pathogenesis of VD remains obscure. It may be related to factors such as cholinergic system damage, altered synaptic plasticity, oxidative stress levels, neuronal apoptosis, inflammatory responses, autophagy, as well as genetic mechanisms (Damodaran *et al.*, 2019; Iadecola, 2010; Wang *et al.*, 2020b; Romay *et al.*, 2019). Acupuncture is an important nonpharmacological therapy that has been gradually accepted by practitioners and patients around the world. Acupuncture is frequently used to treat VD (Du *et al.*, 2018; Ma *et al.*, 2020) and has the advantages of being convenient, safe, and effective. The mechanisms by which acupuncture exerts its effects mainly include inhibition of oxidative stress, neuronal apoptosis and neuroinflammation, regulation of glucose metabolism and neurotransmitters, improvement of synaptic plasticity and blood vessel function (Ye *et al.*, 2017), improvement of cerebral blood flow (Ma *et al.*, 2020), and so on. Nevertheless, exploring the molecular mechanisms by which acupuncture exerts its therapeutic effects may hopefully provide reference materials for improving the therapeutic effects of acupuncture and exploring therapeutic targets for VD. VD, as the only type of dementia that can be prevented, may be reversible if it can be treated early. Therefore, it is extremely important to constantly explore the pathogenesis and treatment modalities of VD.

microRNAs (miRNAs) are a class of non-coding RNAs with 18-25 nucleotides in length that can regulate gene expression. Increased expression of miRNAs, such as miR-134-5p (Liu *et al.*, 2019), miR-210-5p (Ren *et al.*, 2018) and miR-126 (Yu *et al.*, 2019), have been found to be associated with VD. Notably, a study has shown that acupuncture can attenuate inflammation related cognitive impairment by regulating miR-93-mediated signaling pathways (Wang *et al.*, 2020b). miR-143-3p is a potential marker for acute ischemic stroke (Tiedt *et al.*, 2017), which is involved in the regulatory processes of neuronal cell activity (Sun *et al.*, 2020) and neuroinflammation (Du *et al.*, 2019). Notably, these processes are important mechanisms

for the occurrence and development of VD, as well as the functional exertion process of acupuncture treatment. However, the clinical significance of differential expression of miR-143-3p in VD patients and its relationship with acupuncture treatment remain unclear.

Thus, the purpose of this study was to investigate the expression and clinical significance of miR-143-3p in patients with VD, and the role of mir-143-3p in acupuncture treatment of VD. This study shall shed light on the development of therapy for VD.

MATERIALS AND METHODS

Serum sample collection

This study was performed in accordance to the Declaration of Helsinki and the STROBE Statement (https://www.equator-network.org/reporting-guidelines/consort-stricta/) and approved by the Ethics Committee of The Third Hospital of Quzhou (0017289). A total of 106 patients with VD, admitted to The Third Hospital of Quzhou between 2017 and 2020, were enrolled in this study. VD patients were diagnosed according to the National Institute of Neurological Disorders and Stroke-AIREN criteria (NINDS-AIREN) (McVeigh & Passmore, 2006). The inclusion criteria were: 1) patients fulfilled the above diagnostic criteria for VD; 2) patients were younger than 80 years old, and 3) disease duration was more than 2 months. Patients were excluded from this study if they 1) had other neurodegenerative dementia, such as Alzheimer's disease, Huntington disease or Parkinson disease; 2) had cardiovascular and neoplastic diseases; 3) could not cooperate with cognitive function evaluation. Blood samples from VD patients, before and after acupuncture treatment, were collected using disposable vacuum blood collection tube (Zhejiang Gongdong Medical Technology Co., Ltd.) and disposable blood collection needle (SteriLance Medical (Suzhou), lnc.). In addition, 80-year-old- and gender-matched healthy, cognitively normal volunteers, who also underwent physical examination at The Third Hospital of Quzhou at the same time, were recruited as a healthy control group. Their blood samples were also collected. All blood samples were centrifuged to obtain serum and were stored in -80°C ultra-low temperature freezer (Qingdao Haier Biomedical Co., LTD) for further use. Each participant provided a written informed consent.

Evaluation of cognitive function and daily living ability

Before and after acupuncture treatment, the mini-mental state examination (MMSE) and Hasegawa's dementia scale (HDS-R) were used to assess the cognitive function of VD patients, and activities of daily living (ADL) scale was used to assess patients' daily living ability. The specific grading and reference of MMSE scores, HDS-R scores, and ADL scores were as follows.

MMSE scores range from 0 to 30, and the lower the score the worse the cognitive function. MMSE values were recoded as: 24 ≤MMSE score ≤30 is no cognitive impairment; 19 ≤MMSE score ≤23 is mild cognitive impairment; 10 ≤MMSE score ≤18 is moderate cognitive impairment; MMSE score ≤9 is severe cognitive impairment.

HDS-R scores were recoded as: 30 ≤HDS-R score is normal intelligence; 20 ≤ HDS-R score <30 is mildly low intelligence; 10 ≤HDS-R score <20 is moderately low intelligence; HDS-R score <10 is severely low intelligence; HDS-R score <15 is defined as dementia.

ADL scores were recoded as: ADL=100 is living self-care; 60 <ADL score is basic self-care; 40 ≤ADL score ≤60 is living with need for assistance; 20 ≤ADL score <40 is life requires great assistance; ADL score <20 is life completely dependent.

Acupuncture Treatment

Acupuncture is a central component of traditional Chinese medicine (TCM). According to TCM theory, we selected the following major acupoints: GV24 (shenting), EX-HN1 (sishencong), GV20 (baihui), CV17 (tanzhong), PC6 (neiguan), CV6 (qihai), CV12 (zhongwan), ST36 (zusanli), and SP10 (xuehai). In addition, auxiliary acupoints were as follows: ST40 (fenglong), LR3 (taichong), GB20 (fengchi), SP6 (sanyinjiao), and ST25 (tianshu). The used acupoint prescriptions were individualized for each patient and left to the discretion of the acupuncturist. Acupuncture was conducted by licensed acupuncturists with standard stainless steel sterile acupuncture needles (0.3×40 mm, Hwato, China), and needle sensation was elicited by manual stimulation by licensed acupuncturists (Mao *et al.*, 2007). The treatment lasted for 30 minutes every other day for 6 weeks (a total of 21 sessions). The operators who implemented acupuncture in this study were all licensed acupuncturists with more than 5 years of experience performing the interventions and were trained on the specific protocol of this study.

Animals

Adult male Wistar rats (10 weeks of age), purchased from the Vital River Laboratory (Beijing, China), were housed in an environment with a constant room temperature of 25±2°C, a humidity of 60±5%, and a 12 h light/dark cycle. Rats had ad libitum access to food and water. All experiments were performed in accordance to ARRIVE guidelines (https://www.nc3rs.org.uk/arrive-guidelines) and approved by the Institutional Animal Care and Use Committee of The Third Hospital of Quzhou (0217012).

Permanent bilateral common carotid artery occlusion (2VO)

The VD rat model was established using the 2VO method as previously described (Xiao *et al.*, 2018; Wang *et al.*, 2020a). Rats were anesthetized by intraperitoneal injection of 40 mg/kg pentobarbital sodium. The specific procedures were as follows: the rats were safely grasped and immobilized by the left hand; a syringe prepared with pentobarbital sodium anesthetic solution was beveled into the rats' left or right lower ventrolateral quadrant at an angle of approximately 40°C by the right hand, and 40 mg/kg pentobarbital sodium was injected after appropriate needle withdrawal. Bilateral common carotid arteries were separated from the vagus nerve when they were exposed through an abdominal median incision. The bilateral blood vessels were then ligated with 5-0 silk thread. Rats in the sham operation group underwent the same surgery but without arterial ligation. Throughout the surgery, the surgery was as gentle as possible to relieve the animals' pain, and the rats' body temperature was maintained.

Table 1. Baseline characteristics of the study population

Characteristics	Healthy controls (n=80)	VD patients (n=106)	*P*-value
Age	64.4±7.3	66.1±7.9	0.132
Gender			
Female	40	44	0.249
Male	40	62	
Hypertension			
No	46	51	0.205
Yes	34	55	
Diabetes mellitus			
No	49	58	0.372
Yes	31	48	
Coronary heart disease			
No	50	61	0.495
Yes	30	45	
MMSE scores	27.7±1.7	14.4±2.1	< 0.001
HDS-R scores	32.2±1.4	11.5±2.2	< 0.001
ADL scores	80.2±7.2	45.0±7.4	< 0.001

VD, vascular dementia; MMSE, mini-mental state examination; HDS-R, Hasegama's dementia scale; ADL, activities of daily living.

Animal grouping

The rats were randomly divided into six groups: 1) Sham-operated control; 2) 2VO; 3) 2VO+non-acupuncture (acu); 4) 2VO+acu; 5) 2VO+acu+mimic NC; 6) 2VO+acu+miR-143-3p mimic. Rats in the 1) group underwent only sham operation, and the rats in the other groups underwent 2VO operation. In the groups 4–6, disposable sterile acupuncture needles (0.3×40mm, Hwato, China) were penetrated into Baihui (GV-20) and Zusanli bilaterally (ST-36). The needle was twisted 2 times per second for 30 s, respectively. For the rats in group 3, the bilateral hypochondrium was chosen as the acupuncture insertion site (45s of acupuncture). The stimulation duration of rats in group 3 was equal to that of acupuncture rats. Three days after 2VO operation, the rats in groups 3–6 were treated with acupuncture once a day with rest on day 7 for a total of 2 weeks (12 times in total). Meanwhile, for rats in group 5 and 6, miR-143-3p mimic NC and miR-143-3p mimic were injected into rat brains using the intracerebroventricular (ICV) injection method. Rats in groups 5 and 6 received one ICV injection per day for 3 consecutive days. The miR-143-3p mimic NC and miR-143-3p mimic were respectively dissolved in sterile double-distilled water (ddH2O) before use. Then, 5 l volumes (200 pmol/rat) of miR-143-3p mimic NC and miR-143-3p mimic solution were injected into both sides of the lateral ventricle of the corresponding rats. After being anesthetized, the cerebrospinal fluid (CSF) of the rats was collected.

RNA extraction and quantitative real-time PCR (qRT-PCR)

Total RNAs in the serum of participants and CSF of rats were extracted by TRIzol Reagent (Invitrogen, CA, USA). RNA purity and concentration were evaluated using a NanoDrop 2000 (Thermo Fisher Scientific, MA, USA). The cDNA was then synthesized by the reverse transcription of the obtained RNA by a PrimeScript RT reagent kit (TaKaRa, Japan). The qRT-PCR, used to measure the expression levels of miR-143-3p, was conducted by a SYBR Green PCR Master Mix kit (Invitrogen, CA, USA) on a 7500 Real-Time PCR System (Applied Biosystems, USA). miR-143-3p expression was normalized to U6. The final relative miR-143-3p expression was calculated using the $2^{-\Delta\Delta Ct}$ method (Livak & Schmittgen, 2001).

Morris water maze (MWM) test

The cognitive function of rats was evaluated using the MWM test. The MWM pool was 50 cm in depth and 120 cm in diameter, containing water (25±1°C) and a hidden platform. The pool was divided into four quadrants (quadrant I, II, III, and IV). The platform was placed 1 cm below the water surface in quadrant III. The test consists of two main parts, acquisition training and probe trial. Rats were first trained 4 times daily for 5 consecutive days. For training, rats were placed in a random position and allowed 60 s to find the platform and to stay on the platform for 10 s. If the rat failed to find the platform within 60 s, the rat was placed manually on the platform to stay there for 10 s. The escape latency and escape speed were recorded. On day 6, the platform was removed from the pool and a probe tracking was performed. Rats were placed in quadrant I to swim for 60 s. The time spent in the third quadrant and the number of crossings of the platform were recorded.

Statistical analysis

All the statistical analyses were performed by SPSS 22.0 software (IBM Corp.) and GraphPad Prism 7.0 software (GraphPad Software, Inc.). Comparisons in measurement data between two groups and among three groups were conducted by Student's t test and one-way ANOVA followed by Tukey's post hoc test,

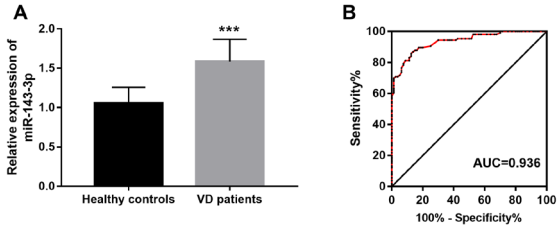

Figure 1. Dysregulation of serum miR-143-3p in patients with VD.
(**A**) Serum miR-143-3p expression in healthy controls and VD patients. (**B**) ROC analysis of miR-143-3p in differentiating between healthy controls and VD patients. ***P<0.001 *vs*. Healthy controls. VD, vascular dementia; AUC, area under the ROC curve; ROC, receiver operating characteristic.

respectively. Chi-square test was used for the comparisons between categorical variables. The diagnostic ability of miR-143-3p was evaluated by receiver operating characteristic (ROC) analysis. Pearson's correlation analysis was used to evaluate the correlation of miR-143-3p with MMSE, HDS-R, and ADL. A P<0.05 indicated statistically significant values.

RESULTS

Baseline characteristics of the study population

The baseline characteristics of the study population were included in Table 1. There was no significant difference between healthy and VD patients in age, gender, hypertension, diabetes mellitus, and coronary heart disease (all P>0.05). In addition, VD patients had significantly lower MMSE, HDS-R, and ADL scores (all P<0.001).

Dysregulation of serum miR-143-3p in patients with VD

As shown in Fig. 1A, serum miR-143-3p expression in VD patients before acupuncture treatment was

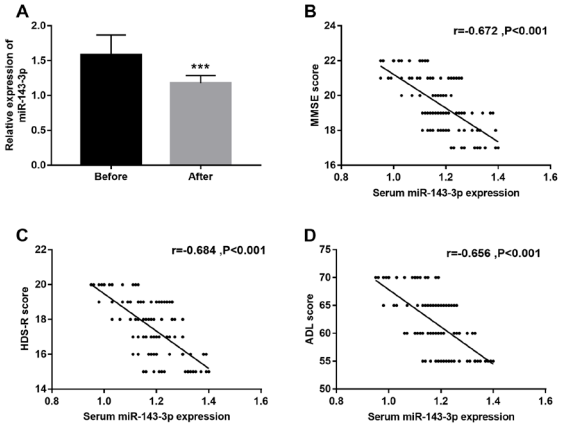

Figure 2. Correlation of serum miR-143-3p with the cognitive function and daily living ability of VD patients after acupuncture therapy.
(**A**) Serum miR-143-3p expression in VD patients before and after acupuncture therapy. (**B**) Correlation of serum miR-143-3p with MMSE scores (r=–0.672, P<0.001). (**C**) Correlation of serum miR-143-3p with HDS-R scores (r=–0.684, P<0.001) **D.** Correlation of serum miR-143-3p with ADL scores (r=–0.656, P<0.001). ***P<0.001 *vs*. Before acupuncture therapy. VD, vascular dementia; MMSE, mini-mental state examination; HDS-R, Hasegama's dementia scale; ADL, activities of daily living.

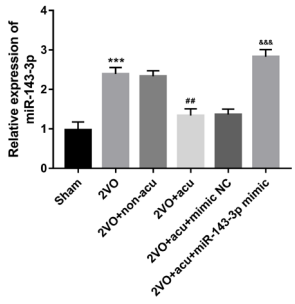

Figure 3. The expression of miR-143-3p was increased by 2VO surgery in rats, and miR-143-3p mimic reversed the inhibitory effects of acupuncture treatment on miR-143-3p levels in 2VO rat model.
***P<0.001 *vs*. Sham; ##P<0.01 *vs*. 2VO; &&&P<0.001 *vs*. 2VO+acu. 2VO, permanent bilateral common carotid artery occlusion; acu, acupuncture treatment; NC, negative control.

Table 2. Correlation of acupuncture therapy with VD patients' cognitive function and daily living ability

	Before therapy	After therapy	*P*-value
MMSE scores	14.4±2.1	19.5±1.5	<0.001
HDS-R scores	11.5±2.2	17.5±1.7	<0.001
ADL scores	45.0±7.4	61.9±5.5	<0.001

VD, vascular dementia; MMSE, mini-mental state examination; HDS-R, Hasegama's dementia scale; ADL, activities of daily living.

significantly increased compared with that in healthy controls (P<0.001). Additionally, serum miR-143-3p had high diagnostic potential in screening VD patients from healthy controls with an area under the ROC curve (AUC) of 0.936 (Fig. 1B). At a cutoff value of 1.265, the sensitivity and specificity are 85.85% and 87.50%, respectively.

Serum miR-143-3p was decreased after acupuncture treatment in VD patients

Then, we investigated the expression of serum miR-143-3p in VD patients before and after acupuncture treatment. After acupuncture treatment, serum miR-143-3p in VD patients was significantly deceased (Fig. 2A, P<0.001).

Correlation of serum miR-143-3p with VD patients' cognitive function and daily living ability after acupuncture therapy

The results in Table 2 showed that MMSE, HDS-R, and ADL scores of VD patients before and after acupuncture treatment changed significantly (all P<0.001), suggesting that the acupuncture treatment improved cognitive function and daily living ability in VD patients. Afterwards, we found the significantly negative correlation of serum miR-143-3p with MMSE scores (Fig. 2B; r=–0.672, P<0.001), HDS-R scores (Fig. 2C; r=–0.684, P<0.001) and ADL scores (Fig. 2D; r=–0.656, P<0.001) of VD patients after acupuncture therapy.

Differentially expressed miR-143-3p in VD animal model

As presented in Fig. 3, after establishing a VD rat model using the 2VO method, the levels of miR-143-3p in the CSF of rats were significantly increased (P<0.001). Additionally, in VD rat model, acupuncture treatment

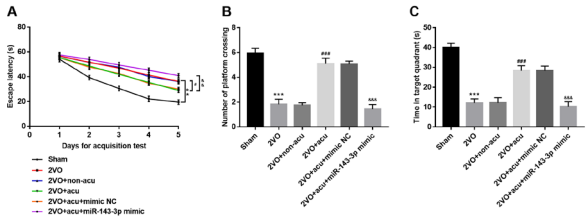

Figure 4. Acupuncture improved the cognitive function of rats through inhibiting miR-143-3p.
(**A**) The escape latency of rats was increased by 2VO surgery, and miR-143-3p overexpression reversed the inhibitory effects of acupuncture treatment on escape latency of 2VO rat model. (**B–C**) The number of platform crossing and time in target quadrant of rats were decreased by 2VO surgery, and the effects of acupuncture treatment on the platform crossing and time in target quadrant of 2VO rat model were reversed by miR-143-3p overexpression. $^{**}P<0.01$, $^{***}P<0.001$ *vs.* Sham; $^{\#}P<0.05$, $^{\#\#\#}P<0.001$ *vs.* 2VO; $^{\&\&}P<0.01$, $^{\&\&\&}P<0.001$ *vs.* 2VO+acu. 2VO, permanent bilateral common carotid artery occlusion; acu, acupuncture treatment; NC, negative control.

significantly decreased miR-143-3p levels ($P<0.01$). Moreover, miR-143-3p mimic reversed the inhibitory effects of acupuncture treatment on miR-143-3p levels in VD rats ($P<0.001$).

Acupuncture improved the cognitive function of rats through inhibiting miR-143-3p

During the training period, 2VO surgery significantly increased the escape latency of the rats (Fig. 4A, $P<0.01$). The platform crossing number and time in target quadrant of rats were decreased by 2VO surgery (Fig. 4B and C, all $P<0.001$). In a VD rat model, the escape latency was decreased, and the number of platform crossing and time in target quadrant were increased after the acupuncture treatment (Fig. 4, all $P<0.05$). Notably, we found that miR-143-3p overexpression reversed the effects of acupuncture treatment on escape latency, number of platform crossing and time in the target quadrant (Fig. 4, all $P<0.01$).

DISCUSSION

An increasing number of studies have demonstrated that abnormally expressed miRNAs play important roles in dementia, including VD. For example, the miR-124/tyrosine-protein phosphatase non-receptor type 1 (PTPN1) signal pathway has been revealed to mediate the synaptic dysfunction and memory deficits in Alzheimer's disease (Wang *et al.*, 2018). miR-153 is elevated in the plasma of dementia patients and rats subjected to 2VO surgery and may serve as a drug target for VD (Yan *et al.*, 2020). Wei and others (Wei *et al.*, 2021) have shown that knockdown of miR-150 improves VD symptoms via regulating the expression of homeobox A1 (HOXA1) *in vivo* and *in vitro*. In addition, abnormal miR-143-3p expression is related to ischemic brain injury (Zhou *et al.*, 2021) and acute ischemic stroke (Tiedt *et al.*, 2017). Moreover, miR-143-3p has regulatory effects on neural cell activity and neuroinflammation (Wang & Liu, 2021, Du *et al.*, 2019). The above studies suggested a potential association between miR-143-3p and VD progression. This study found that the expression of miR-143-3p was upregulated in VD patients. In addition, miR-143-3p was found to be of high diagnostic value for the screening of VD patients. Moreover, aberrant miR-143-3p expression has been shown to be involved in other diseases, such as ovarian cancer (Shi *et al.*, 2018) and deep vein thrombosis (Zhang *et al.*, 2020). Thus, we suggested that the upregulated miR-143-3p might be involved in the progression of VD.

Considering the aberrant expression of miR-143-3p in VD patients and the therapeutic effect of acupuncture on VD patients, we analyzed the relationship between miR-143-3p and acupuncture treatment in VD patients. Previous studies have indicated the regulatory effects of acupuncture treatment on miRNAs, such as miR-222 (Deng *et al.*, 2019), miR-23a-3p (Kong *et al.*, 2021), and miR-19a (Deng *et al.*, 2017). In this study, miR-143-3p expression in VD patients after acupuncture treatment was markedly lower than that in patients before acupuncture treatment, suggesting the inhibitory effect of acupuncture treatment on miR-143-3p. In addition, we confirmed the improvement of cognitive function and daily living ability by acupuncture in VD patients, and we found a negative correlation of miR-143-3p expression with cognitive function and daily living ability in VD patients after acupuncture therapy. Therefore, we speculate that acupuncture might affect the cognitive function and daily living ability in VD *via* regulating miR-143-3p.

A study by Yin et al. revealed that berberine treatment could improve VD in diabetes, which might be achieved by inhibiting miR-133a ectopic expression (Yin *et al.*, 2019). Idebenone treatment has been reported to increase the expression of miR-216a to improve the oxidative stress and neuroinflammation in rats with VD (Qian *et al.*, 2021). The aforementioned studies indicated that some miRNAs could mediate the effects of VD treatment modalities on VD. Notably, acupuncture has been found to mitigate the cognitive impairment associated with inflammation through the regulation of miR-93-mediated signaling pathway **(11)??**. In this study, miR-143-3p expression was found to be markedly increased in the VD rat model. In addition, miR-143-3p upregulation reversed the effects of acupuncture treatment on cognitive function in a rat model of VD. Notably, Yu et al. have found that the reduction of miR-143-3p can attenuate sevoflurane anesthesia induced cognitive impairments (Yu *et al.*, 2021). Thus, acupuncture treatment can ameliorate the cognitive function of VD rats *via* suppressing miR-143-3p expression.

However, there were some limitations. At first, the sample size was small and future studies with a large research cohort are needed. Second, the target genes of miR-143-3p in VD disease were not explored in this study, which need to be further confirmed in future studies. A study has shown that miR-143-3p can regulate neuronal survival by targeting neuregulin-1 (NRG1) in a cellular model of Alzheimer's disease (Sun *et al.*, 2020). Du and others (Du *et al.*, 2019) have found that miR-143/P53-up-regulated modulator of apoptosis (PUMA) axis has a mediating role in microglial activation. Thus, we speculated that miR-143-3p may play a role in VD by targeting NRG1 or PUMA, which needs to be verified in future studies.

In conclusion, the findings indicate that miR-143-3p is increased in patients with VD, is downregulated in VD patients after receiving acupuncture treatment, and acupuncture treatment ameliorates cognitive function of VD via suppressing miR-143-3p. This study provides novel insights into the pathogenesis of VD and a novel target for VD therapy.

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